REMARKS

FORMAL MATTERS:

Claims 1, 3-10, 15 and 16 are pending after entry of the amendments set forth herein.

Claims 1, 3-5, 10, and 16 have been amended. Support for these amendments is found in the claims as originally filed and thought the specification at, for example, Figure 1.

No new matter has been added.

EXAMINER INTERVIEW

Applicants wish to express their gratitude to Examiner Tran and Examiner Paras for the helpful in-person interview on May 8, 2006 with Dr. Richard Schwartz, and by telephone with the undersigned. All outstanding rejections of the claims were discussed during the interview, and particularly the rejection of the claims under §112, ¶1, and §112, ¶2. The present amendments and arguments presented herein reflect those presented during the interview, which amendments and arguments the Examiners indicated may be deemed persuasive to place the application in form for allowance.

WITHDRAWAL OF REJECTIONS

The Applicants express gratitude in the Examiner's indication that prior rejection of claims under 35 U.S.C. §112 and § 102(b) have been withdrawn.

OBJECTIONS TO THE CLAIMS

Claim 10 has been rejected under 37 C.F.R. 1.75(c), for allegedly being improper for failing to further limit the claims. As suggested in the Office Action, Claim 10 has been amended to correct the dependency of the claim to Claim 7. In view of the amendment to claim, this rejection may be withdrawn.

REJECTIONS UNDER §112, ¶1 (WRITTEN DESCRIPTION)

Claims 1, 3-10, 15, and 16 have been rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement. In view of the amendments to the claims and the remarks made here, this rejection is respectfully traversed.

In making the rejection, the Office Action asserts that the "specification disclosure does not sufficiently teach the instant claimed method especially the instant claimed method steps (c) and (d)" (Office Action, page 5). In addition, the Office Action states that the "instant specification description is directed to two distinct methods that are the methods of DNA templeted split 'synthesis' for making subsets of nucleic acid tags...and the method of synthetic coupling reaction of the subsets of nucleic acid tags" (Office Action, page 5).

The Applicants respectfully disagree. As provided in Figure 1 of the patent application and discussed during the Examiner Interview of May 8, 2006, the specification teaches a method of (1) splitting a pool of nucleic acid tags into subsets, (2) reacting each subset with a specific reagent, (3) pooling the reacted nucleic acid tags, (4) splitting the pooled reacted nucleic acid tags into a second group of subsets, and (5) reacting each subset with a specific reagent.

In practicing the claimed method, one starts with a set of pooled nucleic acid tags, wherein each nucleic acid tag includes two or more unique hybridization sequences that will dictate the particular synthetic steps that will be applied to a reaction site carried on each nucleic acid tag.

To carry out the first reaction step, the pool of nucleic acid tags is "split" into a first group of nucleic acids tag subsets, e.g., 10 different subsets corresponding to the ten different sequences (N) at the "first" tag position (V_1) in each tag. This is done by contacting the probes with a first group of solid-phase reagents (immobilized sequences), each having a sequence that is complementary to one of the N different hybridization sequences in the "first-position" of the nucleic acid tags. In other words, the tags are divided into N subsets, where each subset is determined by the hybridization sequence in the "first-position" of the nucleic acid tags. This step is detailed, for example, on page 14, line 7 to page 15, line 8 and on page 1 of Exhibit A.

After this splitting step, the N different nucleic acid tag subsets, e.g., ten different subsets of nucleic acid tags, are reacted with N different reagents, where the identity of each reagent is known (dictated by) the particular nucleic acid tag subset. This first coupling step, converts the chemical

reaction site of each nucleic tag to a reagent-specific compound intermediate (see page 15, line 25 to page 16, line 18, and page 1 of Exhibit A).

Following the first reaction step, the reacted nucleic acid tags are pooled and then contacted with a second group of solid-phase reagents (immobilized sequences), each having a sequence that is complementary to one of the N different hybridization sequences in the "second-position" of the nucleic acid tags. As above, this step again splits the tags into a given number of subsets, e.g., 10 subsets, where each subset is now determined by the hybridization sequence in the "second-position" of the nucleic acid tags (see page 15, lines 9-15, and page 2 of Exhibit A).

Each of the different subset of reacted nucleic acid tags are then reacted with one of a second plurality of reagents, a different one for each subset, as disclosed, for example, on page 16, lines 24 and 25, for split and combine methods of synthesis, as described additionally on page 11, lines 3-17 (see also Figure 1 of patent application and page 2 of Exhibit A).

This process of splitting the previously reacted nucleic acid tags into N different subsets, by hybridizing the tags with a new set of immobilized oligonucleotides, then reacting the N new subsets of nucleic acid tags with N different selected reagents, is repeated until all of the reaction steps to be performed successively on the tag reaction sites are complete, as described on page 16, lines 24-25 (see also pages 3-4 of Exhibit A).

In the sprit of expediting prosecution and without conceding to the correctness of the rejection, Clam 1 has been amended for clarity to recite in step (a) that the group of subsets of nucleic acid tags is formed "from a pool of nucleic acid tags" and that at the end of step (b) "subsets of reacted nucleic acid tags" are produced. In addition, the claim has been amended to include an additional step between original steps (b) and (c) that recites "**pooling the subsets of reacted nucleic acid tags**" and an amendment to original step (c) to recite "forming a second group of subsets of the **pooled reacted** nucleic acid tags".

As such, in view of the amendments to the claims and the remarks made herein, this rejection may be withdrawn.

REJECTIONS UNDER §112, ¶2 (INDEFINITENESS)

Claims 1, 3-10, 15, and 16 (Office Action, page 9)

Claims 1, 3-10, 15, and 16 have been rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention. The Office Action on pages 9-12 lists five particular aspects to the rejection. Each item is addressed in detail below.

Item A (Office Action, page 9):

The Office Action indicates that step (a) of claim 1 is allegedly vague and indefinite because it "is unclear as to how the 'second hybridization sequences' appear in this claimed subset of nucleic acid tags produced by instant step (a) of claim 1 since the reaction is between the '*first hybridization sequences*' of the claimed '*nucleic acid tag*' and the '*first immobilized sequence*'" (Office Action, page 10, emphasis in original).

The Applicants note that in practicing the claimed method, one starts with a set of pooled nucleic acid tags, wherein each nucleic acid tag includes two or more unique hybridization sequences that dictate the particular synthetic steps that will be applied to a reaction site carried on each nucleic acid tag (e.g., as described on page 12, line 22 to page 13, line 23, each nucleic acid tag may include ten different hybridization sequences V_1-V_{10}) (see also, Exhibit A, page 1).

To carry out the first reaction step, the pool of nucleic tags are "split" into a first group of nucleic acid tag subsets, e.g., 10 different subsets corresponding to the ten different hybridization sequences (N) at the "first" tag position (V_1) in each tag. This is done by contacting the nucleic acid tags with a first group of solid-phase reagents (immobilized sequences), each having a sequence that is complementary to one of the N different "first-position" hybridization sequences in the nucleic acid tags. In other words, the nucleic acid tags are divided into N subsets, where each subset is determined by the "first-position" hybridization sequence of the nucleic acid tags (e.g., as described on page 14, line 7 to page 15, line 8). As a result, within each subset the nucleic acid tags will have the same "first hybridization sequence". However, the nucleic acid tags within the same subset will have different "second hybridization sequences".

In the spirit of expediting prosecution and without conceding to correctness of the rejection, Claim 1 has been amended to remove the objectionable language and to recite "forming a first group of subsets of nucleic acid tags for participating in a first synthetic reaction step **from a pool of nucleic acid tags**, wherein each nucleic acid **tag** comprises a first hybridization sequence linked to a second hybridization sequence, which said second hybridization sequence is linked to a chemical reaction site, by contacting said nucleic acid tags with a plurality of first immobilized nucleotide sequences, each designed to capture a subset of said **nucleic acid** tags by hybridization between one of said first hybridization sequences and the first immobilized sequence".

As such, in view of the amendment to the claim, this rejection may be withdrawn.

Item B (Office Action, page 10):

The Office Action indicates that step (a) of claim 1 is allegedly vague and indefinite because it "is unclear as how the '*second hybridization sequences*' and '*chemical reaction site*' appear in this claimed subset of nucleic acid produce[d] by instant step (a) of claim 1 since the reaction is between the '*first hybridization sequences*' of the claimed 'nucleic acid tag' and the '*first immobilized sequence*'" (Office Action, page 11, emphasis in original).

As noted above, one starts with a set of pooled nucleic acid tags, wherein each nucleic acid tag includes two or more unique hybridization sequences (referred to a the "first hybridization sequence" and the "second hybridization sequence", etc.) and a chemical reaction site (see Figure 1 of the patent application).

As a result of the first splitting step, the pool of nucleic tags are divided into a first group of nucleic acids tag subsets by hybridization between the first hybridization sequences of the nucleic acid tags and the first immobilized sequences. Within each subset the nucleic acid tags will have the same "first hybridization sequence" and will have different "second hybridization sequences". In addition, all the nucleic acid tags will have a chemical reaction site (see e.g., Figure 1 of the patent application and page 1 of Exhibit A). Therefore, the Applicants maintain that presence of the second hybridization sequences and the chemical reaction site in the claimed subsets is clear.

As such, in view of the remarks made above, this rejection maybe withdrawn.

Item C (Office Action, page 11):

The Office Action indicates that step (b) of claim 1 is allegedly vague and indefinite because it "is unclear how '*the chemical reaction site in each tag*' is converted to '*a reagent-specific compound intermediate on the nucleic acid tag in each subset*' when the product produce[d] from instant claimed step (a) is a subset of hybridized nucleotide sequences between the '*first hybridization sequences*' of the claimed '*nucleic acid tag*' and the '*first immobilized sequence*'" (Office Action, page 11, emphasis in original).

As noted above, following the first splitting step, the pool of nucleic tags are divided into a first group of nucleic acids tag subsets. Within each subset the nucleic acid tags will have the same "first hybridization sequence" and will have different "second hybridization sequences". In addition, all the nucleic acid tags will have a chemical reaction site (see e.g., Figure 1 of the patent application and page 1 of Exhibit A).

In the spirit of expediting prosecution and without conceding to correctness of the rejection, Claim 1 has been amended for clarity to recite "reacting the chemical reaction sites **of the nucleic acid tags** in each of the subsets formed in (a) with a selected one of a plurality of first reagents to convert the chemical reaction site **of each subset of nucleic acid** tag to a reagent-specific compound intermediate **to produce subsets of reacted nucleic acid tags**".

As such, in view of the amendments to the claims and remarks made above, this rejection maybe withdrawn.

Item D (Office Action, page 12):

The Office Action indicates that step (c) of claim 1 is allegedly vague and indefinite because it is "unclear how the product produced in step (b) would hybridize to the '*second immobilized sequence*'" since "the product produced in step (b) is a '*reagent specific compound intermediate*', which results

from converting the '*chemical reaction site*' with the '*first reagent*'" (Office Action, page 12, emphasis in original).

As noted above, following the first splitting step, the pool of nucleic tags is divided into a first group of nucleic acids tag subsets based on the "first hybridization sequences". Within each subset the nucleic acid tags will have the same "first hybridization sequence", a different "second hybridization sequence", and a chemical reaction site (see e.g., Figure 1 of the patent application and page 1 of Exhibit A). The chemical reaction sites of the nucleic acid tags in each of the subsets are then reacted with a plurality of reagents to produce subsets of reacted nucleic acid tags (see Exhibit A, page 1). The reacted nucleic acid tags are then divided into a second group of subsets based on the "second hybridization sequences" (see e.g., Figure 1 of the patent application and page 2 of Exhibit A).

However, in the sprit of expediting prosecution and providing clarity to the claims, Clam 1 has been amended at the end of step (b) to recite that "subsets of reacted nucleic acid tags" are produced. In addition, the claim has been amended to include an additional step between original steps (b) and (c) that recites "**pooling the subsets of reacted nucleic acid tags**" and an amendment to original step (c) to recite "forming a second group of subsets of the **pooled reacted** nucleic acid tags".

As such, in view of the amendments to the claims and remarks made above, this rejection maybe withdrawn.

Item E (Office Action, page 12):

The Office Action indicates that step (d) of claim 1 is allegedly vague and indefinite because it is "unclear how the product produced in step (c) would react with a plurality of second reagents since the product produced in step (c) is the hybridized nucleotide sequences between the '*second hybridization sequences*' and the '*second immobilized sequence*'" (Office Action, page 12, emphasis in original).

In the sprit of expediting prosecution and providing clarity to the claims, Clam 1 has been amended to recite that the result of original step (c) (step (d) in currently amended form) is a "second group of subsets of the **pooled reacted** nucleic acid tags". In addition, original step (d) (step (e) in

currently amended form) has also been amended for clarity to simply recite "carrying out the second synthetic step by reacting the **reacted** nucleic acid tag in each of the subsets formed in **(d)**".

As such, in view of the amendments to the claims and remarks made above, this rejection maybe withdrawn.

Claim 10 (Office Action, page 13)

Claim 10 has been rejected under 35 U.S.C § 112, for allegedly providing insufficient antecedent basis for claim limitations. As suggested in the Office Action, Claim 10 has been amended to correct the dependency of the claim to Claim 7. In view of the amendment to claim, this rejection may be withdrawn.

REJECTIONS UNDER §112, ¶2 (OMISSION OF STEPS)

Claims 1, 3-10, 15, and 16 (Office Action, page 13)

Claims 1, 3-10, 15, and 16 have been rejected under 35 U.S.C. § 112, second paragraph, for allegedly being incomplete for omitting an essential step. In particular, the Office Action asserts that a step between claimed steps (b) and (c) has been omitted. In view of the amendments to the claims and the remarks made herein, this rejection is respectfully traversed.

The Office Action asserts that

> "[t]here is a gap between steps (b) and (c) because in this case the product produce[d] in step (b) is a reagent-specific compound intermediate and yet in step (c) the product is a subset of hybridized nucleotide sequences between the '*second hybridization sequences*' and the '*second immobilized sequence*'. It is unclear as to what happen[s] to the product produce[d] in step (b)...and/or how it is the 'starting' material to produce the product of step (c)..."

(Office Action, page 13, emphasis in original).

In the sprit of expediting prosecution and without conceding to the correctness of the rejection, Clam 1 has been amended for clarity to recite that at the end of step (b) "subsets of reacted nucleic acid tags" are produced. In addition, the claim has been amended to include an additional step between original steps (b) and (c) that recites "**pooling the subsets of reacted nucleic acid tags**" and an

amendment to original step (c) to recite "forming a second group of subsets of the **pooled reacted** nucleic acid tags".

As such, the amendments provide how the product produced in original step (b) is then used in original step (c) (step (d) in currently amended form). Therefore, in view of the amendments to the claims, this rejection may be withdrawn.

Claims 1, 3-10, 15, and 16 (Office Action, page 14)

Claims 1, 3-10, 15, and 16 have been rejected under 35 U.S.C. § 112, second paragraph, for allegedly being incomplete for omitting an essential step. In particular, the Office Action asserts that a step between claimed steps (c) and (d) has been omitted. In view of the amendments to the claims and the remarks made herein, this rejection is respectfully traversed.

The Office Action asserts that:

> "[t]here is a gap between steps (c) and (d) because in this case the product produce[d] in step (c) is the hybridized nucleotide sequences between the 'second hybridization sequences' and the '*second immobilized sequences*' and **not** '*the reagent-specific compound intermediate*' as claimed in step (d). It is unclear as to what happene[d] to the product produce[d] in step (c) ... and how does step (c) produce the 'starting' material of the '*reagent specific compound intermediate*' as claimed in step (d)..."

(Office Action, page 14, emphasis in original).

In the sprit of expediting prosecution and without conceding to the correctness of the rejection, Clam 1 has been amended for clarity to recite that the result of original step (c) (step (d) in currently amended form) a "second group of subsets of the **pooled reacted** nucleic acid tags". In addition, original step (d) (step (e) in currently amended form) has also been amended for clarity to simply recite "carrying out the second synthetic step by reacting the **reacted** nucleic acid tag in each of the subsets formed in **(d)**".

As such, the amendments provide how the product produced in original step (c) (step (d) in currently amended form) is then used in original step (d) (step (e) in currently amended form). Therefore, in view of the amendments to the claims, this rejection may be withdrawn.

CONCLUSION

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number STAN-390.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: June 1, 2006

By: _____
Edward J. Baba
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Enclosure(s):

- Exhibit A (pages 1-4).

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